DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20903

May 2, 2009

Richard E. Besser, MD
Acting Director
Centers for Disease Control and Prevention
1600 Clifton Road, MS C-12
Atlanta, GA 30333
Clifton, Bldg. 1, Room 6430

Dear Dr. Besser:

On April 27, 2009, FDA issued a letter authorizing the emergency use of the Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) for the presumptive diagnosis of swine influenza A (H1N1), pursuant to section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. § 360bbb-3) by public health and other qualified laboratories. On May 1, 2009, CDC submitted a request for an amendment to the Emergency Use Authorization. In response to that request, the letter authorizing emergency use of the rRT-PCR Swine Flu Panel is being reissued in its entirety with the amendments, as requested by CDC, incorporated.[1]

On April 26, 2009, pursuant to section 564(b)(1)(C) of the Act (21 U.S.C. § 360bbb-3(b)(1)(C)), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency under 42 U.S.C. § 247d that affects, or has a significant potential to affect, national security, and that involves a specified biological, chemical, radiological, or nuclear agent or agents, or a specified disease or condition that may be attributable to such an agent or agents -- in this case, swine influenza A (H1N1).[2] Pursuant to section 564(b) of the Act (21 U.S.C. § 360bbb-3(b)), and on the basis of such determination, the Secretary of the Department of Health and Human Services then declared an emergency justifying the authorization of the emergency use of the Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) subject to the terms of any authorization issued under 21 U.S.C. § 360bbb-3(a).

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act (21 U.S.C. § 360bbb-3(c)) are met, I am authorizing the emergency use of the Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel)[3] for the presumptive diagnosis of swine influenza A (H1N1) virus infection in human individuals who

[1] The amendments to the April 27, 2009 letter allow use of different sample types (throat swabs (TS), dual NPS/TS swab, or nasal aspirate (NA) specimens) and different reagents.
[2] Memorandum, Determination Pursuant to § 564 of the Federal Food, Drug, and Cosmetic Act (April 26, 2009).
[3] FDA is authorizing the emergency use of the Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) as described in the scope section of this letter (Section II). For ease of reference, this letter will use the term the " rRT-PCR Swine Flu Panel."

have been diagnosed with influenza A caused by a virus not subtypeable by currently available FDA-cleared devices, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the rRT-PCR Swine Flu Panel for the presumptive diagnosis of swine influenza A (H1N1) virus infection for human individuals who are diagnosed with influenza A caused by a virus that is not subtypeable by currently available FDA-cleared devices meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

(1) The recently isolated novel 2009 influenza A (H1N1), or swine flu, virus can cause influenza, a serious or life threatening disease or condition to humans infected by this virus;

(2) based on the totality of scientific evidence available to FDA, it is reasonable to believe that the rRT-PCR Swine Flu Panel may be effective in the presumptive diagnosis of swine influenza A (H1N1) virus infection, and that the known and potential benefits of the rRT-PCR Swine Flu Panel, when used in the presumptive diagnosis of swine influenza A (H1N1) virus infection, outweigh the known and potential risks of such products; and

(3) there is no adequate, approved, and available alternative to the emergency use of the rRT-PCR Swine Flu Panel for the presumptive diagnosis of swine influenza A (H1N1) virus infection.[4]

Therefore, I have concluded that the emergency use of the rRT-PCR Swine Flu Panel for the presumptive diagnosis of swine influenza A (H1N1) virus infection in human individuals who are diagnosed with influenza A infections not subtypeable by currently available FDA-cleared devices meets the above criteria for issuance of an authorization.

II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the use of the authorized rRT-PCR Swine Flu Panel for the presumptive diagnosis of 2009 H1N1 influenza A virus infection for individuals who are diagnosed with influenza A caused by a virus not subtypeable by currently available FDA-cleared devices.

The authorized rRT-PCR Swine Flu Panel is as follows:

The Swine Influenza Virus Real-time RT-PCR Detection Panel is a panel of oligonucleotide primers and dual-labeled hydrolysis (Taqman®) probes for use in the real-time RT-PCR assay on the ABI 7500 Fast Dx Real-Time PCR instrument for the *in vitro* qualitative detection of 2009 H1N1 influenza viral RNA in nasopharyngeal swabs

[4] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

(NPS), nasal swabs (NS), throat swabs (TS), dual NPS/TS swab, or nasal aspirate (NA) specimens from patients with signs and symptoms of respiratory infection and viral culture. The universal 2009 H1N1 influenza swInfA (NP gene) and swH1 (HA gene) primer and probe sets are designed for detection of 2009 A/H1N1 influenza viruses. In addition rRT-PCR Flu Panel (**NPS, NS, TS, NPS/TS, NA**) authorized for emergency use utilizes the AgPath-ID™ One-Step RT-PCR Kit Human amplification reagents.

The rRT-PCR Swine Flu Panel includes the following primer and probe sets:

- **InfA** detects universal influenza A strains in nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), dual NPS/TS swab, or nasal aspirate (NA) specimens from patients with signs and symptoms of respiratory infection, and virus culture.
- **swInfA** specifically detects swine influenza A strains (NP gene) in nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), dual NPS/TS swab, or nasal aspirate (NA) specimens from patients with signs and symptoms of respiratory infection, and virus culture.
- **swH1** is specific for swine influenza A, subtype H1 (HA gene) in nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), dual NPS/TS swab, or nasal aspirate (NA) specimens from patients with signs and symptoms of respiratory infection, and viral culture.

The rRT-PCR Swine Flu Panel also includes control materials:

- **RNase P (RP)** detects human RNase P and is used as a positive control with human clinical specimens to indicate that adequate isolation of nucleic acid resulted from the extraction of the clinical specimen.
- **Swine Influenza Panel Real-Time RT-PCR Positive Control (SIPC)** is a positive control designed to react with all the primer and probe sets including RNase P.

The above rRT-PCR Swine Flu Panel, when labeled consistent with the attached template is authorized to be distributed to public health and other qualified laboratories[5] under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

The following written information pertaining to the emergency use of the authorized rRT-PCR Swine Flu Panel is authorized to be made available to health care providers and patients:

- Fact Sheet For Healthcare Providers: Interpreting Swine Influenza Rt-Pcr Detection Panel Test Results
- Fact Sheet For Patients: Understanding Swine Influenza Kit Test Results

See attached. As described in section IV below, CDC and the appropriate state and/or local public health authority(ies) are also authorized to make available additional information relating

[5] All users, analysts, and any person reporting diagnostic results from use of this device should be trained to perform and interpret the results from this procedure by a CDC instructor or designee prior to use. CDC Influenza Division will limit the distribution of this device to those users who have successfully completed training provided by CDC instructors or designees. Use is limited to designated laboratories that are qualified to receive and use the CDC rRT-PCR Flu Panel (IVD) 510(K) 080570. See "Conditions of Authorization" below.

to the emergency use of the authorized rRT-PCR Swine Flu Panel that is consistent with, and does not exceed, the terms of this letter of authorization.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the authorized rRT-PCR Swine Flu Panel in the specified population, when used in the presumptive diagnosis of swine influenza A (H1N1) virus infection, outweigh the known and potential risks of such product.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, that it is reasonable to believe that the authorized rRT-PCR Swine Flu Panel may be effective in the presumptive diagnosis of swine influenza A (H1N1) virus infection pursuant to section 564(c)(2)(A) of the Act. FDA has reviewed the scientific information available including the information supporting the conclusions described in Section I above, and concludes that the authorized rRT-PCR Swine Flu Panel, when used to presumptively diagnose swine influenza A (H1N1) virus infection in the specified population, meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized rRT-PCR Swine Flu Panel under this EUA must be consistent with, and may not exceed, the terms of this letter, including the scope and the conditions of authorization set forth below. Subject to the terms of this EUA and under the circumstances set forth in the Secretary of HHS's determination under section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the rRT-PCR Swine Flu Panel described above is authorized to presumptively diagnose swine influenza A (H1N1) virus infection in human individuals who are diagnosed with influenza A caused by a virus not subtypeable by currently available FDA cleared devices.
This EUA will cease to be effective when the declaration of emergency is terminated under section 564(b)(2) of the Act or when the EUA is revoked under section 564(g) of the Act.

III. Waiver of Certain Requirements

I am waiving the following requirements for the rRT-PCR Swine Flu Panel during the duration of this emergency use authorization:

- current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the rRT-PCR Swine Flu Panel;
- registration and listing requirements under section 510 of the Act;
- labeling requirements for cleared, approved, or investigational devices, including labeling requirements under 21 CFR 809.10 and 809.30, except for the intended use statement (21 CFR 809.10(a)(2), (b)(2)), adequate directions for use (21 U.S.C. 352(f)), (21 CFR 809.10(b)(5) and (8)), any appropriate limitations on the use of the device including information required under 21 CFR 809.10(a)(4), and any available information regarding performance of the device, including requirements under 21 CFR 809.10(b)(12);
- investigational device requirements, including requirements under 21 CFR Part 812; and
- reporting requirements that apply to cleared or approved devices, including requirements under 21 CFR Parts 803 and 806.

IV. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

CDC

A. CDC will distribute the rRT-PCR Swine Flu Panel labeled with the intended use statement, adequate directions for use, any appropriate limitations on the use of the device, and any available information regarding performance of the device only to qualified laboratories.

C. CDC will provide to the qualified state and/or local public health authority(ies) the authorized rRT-PCR Swine Flu Panel Fact Sheets for health care providers, and the authorized rRT-PCR Swine Flu Panel Fact Sheets for patients.

D. CDC will make available on its website the authorized rRT-PCR Swine Flu Panel Fact Sheets for health care providers, and the authorized rRT-PCR Swine Flu Panel Fact Sheets for patients.

E. CDC will ensure that the state and/or local public health authority(ies) are informed of this EUA, including the terms and conditions herein.

F. CDC will ensure qualified laboratories have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.

G. CDC will track adverse events.

H. Through a process of inventory control, CDC will maintain records of device usage.

I. CDC will collect information on the performance of the assay, to include the incidence of false positive and negative results.

Public Health and Other Qualified Laboratories

J. Qualified laboratories will perform the assay on an Applied Biosystems 7500 Fast Dx Real-time PCR instrument or the RUO marketed Applied Biosystems 7500 Real-time PCR instrument that is validated by Applied Biosystems with regard to the updated software but only partially qualified regarding its laboratory performance (proficiency testing with the CDC sample panel not performed).

K. Qualified laboratories will have a process in place for reporting test results to health care providers and federal, state and/or local public health authorities, as appropriate.

CDC andstate and/or Local Public Health Authority(ies)

M. CDC and the appropriate state and/or local public health authority(ies) are authorized to make available additional information relating to the emergency use of the authorized rRT-PCR Swine Flu Panel that is consistent with, and does not exceed, the terms of this letter of authorization.

N. Only CDC may request changes to the authorized Fact Sheet for health care providers or the authorized rRT-PCR Swine Flu Panel Fact Sheet for patients. Such requests will be made by contacting FDA concerning FDA review and approval.

O. CDC and the appropriate state/and or local public health authority(ies) will ensure that records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

The emergency use of the authorized rRT-PCR Swine Flu Panel as described in this letter of authorization must comply with the conditions above and all other terms of this authorization.

V. Duration of Authorization

This EUA will be effective until the declaration of emergency is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

5/2/19

Joshua M. Sharfstein, MD
Principal Deputy Commissioner
Acting Commissioner

Attachments
1. Fact Sheet For Healthcare Providers: Interpreting Swine Influenza RT-PCR Detection Panel Test Results
2. Fact Sheet For Patients: Understanding Swine Influenza Kit Test Results
3. Swine Influenza Virus Real-time RT-PCR Detection Panel (rRT-PCR Swine Flu Panel) Labeling